Section 2:

Non-technical Abstract

HIV infection leads to destruction of a person's immune system, primarily through loss of T-lymphocytes. These and other important cells of the immune system are constantly being generated from specialized progenitor cells found in the bone marrow. In HIV infected persons, these progenitor cells cannot produce new T-lymphocytes as fast as they are killed by the HIV virus. This is the second in a series of studies that ask if genetically engineered progenitor cells can give rise to T-lymphocytes that are less likely to be killed by infection with HIV. In this study, we will use the same procedure for obtaining and genetically engineering progenitor cells that we used in our first study (BB-IND 6946). Basically, progenitor cells will be made to leave the bone marrow and enter the blood stream by the use of a stimulatory drug. Progenitor cells will then be obtained from a blood sample obtained by a procedure similar to a blood donation. These progenitor cells will be cultured for 3 days on other cells previously obtained from the person's bone marrow. The progenitor cells will then be genetically engineered by treatment with a modified retrovirus that carries a gene encoding for two ribozymes. The retrovirus does not contain any virus genes, is not capable of replicating or spreading to other cells and is not related to the HIV virus. The ribozymes are a special type of RNA capable of finding and destroying HIV RNA. Cells that contain these ribozymes may be protected from HIV infection. Additional progenitor cells will be treated with a similar retrovirus, but lacking the ribozyme gene. The engineered cells will then be given back to the patient in a manner similar to a blood infusion. In the first study we obtained, engineered, and returned these progenitor cells to HIV infected volunteers who were otherwise healthy. In this study we will be testing the safety, engraftment, and survival of these cells in patients who are being treated for AIDS-related lymphoma. The treatment involves standard chemotherapy for AIDS lymphoma, followed by an additional treatment called stem cell transplantation or SCT. Only persons who respond to the initial chemotherapy, and who have a >100 CD4 lymphocyte count, will be eligible to receive SCT. Two-thirds of the isolated progenitor cells will be genetically engineered with the retrovirus that contains the ribozyme-gene and the control retrovirus. One-third of the PBPC will not have any genetic change in order to assure that the SCT is not altered by the genetic manipulation. This study will determine whether the genetically modified PBPC can grow and make new blood cells after SCT and whether survival of the ribozyme-bearing cells is different than the control cells. In addition, the study will evaluate the toxicity and disease-free survival of persons undergoing high dose chemotherapy with SCT for AIDS lymphoma.